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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,667	01/18/2001	Nobuyuki Ise	201803US0DIV	9063

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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,667	Ise	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 10-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 10-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/773,106.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The preliminary amendments filed on 1-18-2001 and 5-10-2002 have been entered into the record. The preliminary amendment on the transmittal papers regarding continuing data could not be entered since the format of the transmittal request precludes clear the entry of the appropriate information. Claims 10-22 are pending. Claims 1-9 have been canceled.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 08/773,106, filed on 12-26-96.

It is noted that this application appears to claim subject matter disclosed in prior Application No. 08/773,106, filed 12-26-96. It is noted that the claim for priority to 08/773,106 was made in the transmittal papers which requested amendment of the first line of the specification. However, the format of the transmittal request precludes clear the entry of the appropriate information. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a) and should reflect the current status of all nonprovisional parent applications referenced should be included. and (a)(5)(ii).

Drawings

The formal drawings were receive 4-18-01. These drawings are approved by the draftsperson.

Information Disclosure Statement

The information disclosure/related case statement under 37 CFR 1.97, filed 5-21-01, that discloses the related application 08/773,106 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the preamble recites an assay for detection of anti-*Treponema pallidum* antibodies wherein the only step is reacting a fused antigen with a sample in which the antibodies are to be detected. The assay is incomplete because it fails to detect the presence or absence of antibodies and lacks a correlation step. What is the outcome of "reacting" ? What is reacting and the product of the "reaction" and how does the reaction relate to the assay. Where is the detection of the "reaction product"? In the absence of a detection step of the antibody-fused antigen reaction product the assay can not presumably function to achieve the coal of the preamble "an assay for anti-*Treponema pallidum* antibodies". As such, the claims do not recite a

complete assay method that detects the presence or absence of antibodies that bind and "the reaction" is unclear since it is not specifically defined in the claims as a binding event between the antibodies and the fused antigen as opposed to a catalytic antibody reaction which is enzymatically based. As such, the assay is incomplete and the metes and bounds of "reacting" are not clear since this term in the catalytic antibody art is used represent a chemical reaction.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10, 11, 12, 13, 14, 15, 19, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujimura et al (EP 0670494 A2, 06 September 1995) in view of Schinnick et al (US Patent No. 4,976,958), Dunn et al (WO 95/12676, May 11, 1995) and Flavell et al (WO 95/04145, Feb. 9, 1995).

Fujimura et al teach that the 15, 17 and 47-kilodalton proteins are antigenic, in that infected individuals have an antibody response to these surface proteins. Fujimura et al teach that the 15/17 combination is a more sensitive diagnostic reagent than the 47 kDa antigen alone. Fujimara et al teach that antigens having various molecular weights are present on the surface of Treponema pallidum and these antigens have molecular weights of 47 kDa, 42 kDa, 17 kDa and 15 kDa. Fujimara et al teach that the genes of the 47 Kda, 17 Kda and 15 kDa surface antigens have been cloned and produced by biotechnology and the amino acid sequences established (see page 3, lines 1-10). Fujimara et al teach fusion proteins comprising membrane antigens of *T. pallidum* which a molecule are weights of 15 and 17 fused to glutathione S-transferase (GST) for use in immunoassays to detect anti-T. pallidum antibodies that bind the surface antigens (page 11, claims 1-3). Fujimura et al discloses that the 15, 17 and 47-kilodalton proteins used in immunoassays are surface antigens of *T. pallidum* (see page 2, line 57-page 3, line 1).

Schinnick et al teaches using a polymer of repeating *Mycobacterium tuberculosis* peptide units for use in an immune assay (see column 5).

Dunn et al teach chimeric *Borrelia* proteins (i.e. the instant fused antigen) consisting of at least two antigenic polypeptides from corresponding and/or non-corresponding proteins from the same and/or different species. Dunn et al teach that these chimeric proteins are useful as immunodiagnostic reagents.

Flavell et al teach that the antigenic polypeptides maybe expressed as fusion proteins and multimeric proteins from *Borrelia* (page 23, lines 5-11) for the objective of increasing stability or rendering the molecules more amenable to purification and preparation.

It would have therefore been prima facie obvious to one of ordinary skill in the art at the time the invention was made, to make repeating homopolymers of the known *T. pallidum* surface antigens 15, 17 or 47-kilodalton antigens of Fujimura et al because each of Schinnick et al, Dunn et al and Flavell et al teach that homomeric/multimeric proteins are useful as assay reagents, increase the stability of the molecules and may render the molecules more amenable to purification and preparation and Fujimura et al teach that each of the 15, 17 and 47 kDa surface antigens have been cloned and produced by biotechnology. As to claims 10, 11, 12, 13, 14, 15, 19, 21 and 22 it would have therefore been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, to make repeating heteropolymers of the known *T. pallidum* surface antigens 15, 17 or 47-kilodalton antigens of Fujimura et al because each of Schinnick et al, Dunn et al and Flavell et al teach that chimeric antigenic proteins are useful as assay reagents, increase the stability of the molecules and may render the molecules more amenable to purification and preparation. While none of the references teaches fusing specifically two, three or four of the 15, 17 and 47-kilodalton antigens together as recited, one of ordinary skill in the art would have been expected to optimize the number and arrangement of linked hetero units in the heteropolymer to provide for a highly sensitive assay for the detection of antibodies or *T. pallidum per se*. One would have been motivated to combine the 15 and 17 Kda antigens in a heteropolymer/chimera because Fujimura et al teach that the combination of the 15 and 17 antigen as a fusion product provides for a more sensitive assay than the products alone. One of ordinary skill in the art would have readily appreciated the broad applicability of chimeric heteropolymers or homopolymers for use in immune assays.

Claims 16, 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujimura et al (EP 0670494 A2, 06 September 1995), Schinnick et al (US Patent No. 4,976,958), Dunn et al (WO 95/12676, May 11, 1995) and Flavell et al (WO 95/04145, Feb. 9, 1995) as applied to claims 10, 11, 12, 13, 14, 15, 19, 21 and 22 above, and further in view of Weigel et al (Infection and Immunity, 60(4):1568-76, 4/92).

Fujimura et al (EP 0670494 A2, 06 September 1995), Schinnick et al (US Patent No. 4,976,958), Dunn et al (WO 95/12676, May 11, 1995) and Flavell et al (WO 95/04145, Feb. 9, 1995) are set forth supra. The combination as combined differs by not fusing the 47-kilodalton protein to itself or to either or both of the 15 and 17-kilodalton antigens.

Weigel et al teach that the 47 kDa surface antigen is useful in a serological test for syphilis (see page 1575) and teaches that the antigen is highly immunogenic or pathogenic (page 1568). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the 47-kilodalton protein for either the 15 or 17-kilodalton peptide in the homopolymer or heteropolymer as combined *supra* because Weigel et al and Fujimura et al teach that the 15, 17 and 47 kilodalton antigens are useful to detect *T.*

pallidum. While none of the references teaches fusing specifically two, three or four of the 15, or 17- in combination with the 47-kilodalton antigen together as recited, one of ordinary skill in the art would have been expected to optimize the number and arrangement of linked hetero units in the heteropolymer to provide for a highly sensitive assay for the detection of antibodies or *T. pallidum per se*. While none of the references teaches fusing specifically two, three or four of the same 47-kilodalton antigen together as recited, one of ordinary skill in the art would have been expected to optimize the number of linked units in the homopolymer to provide for a highly sensitive assay for the detection of antibodies or *T. pallidum per se*.

Claims 10, 11, 12, 13, 14, 15, 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weigel et al (Infection and Immunity, 60(4):1568-76, 4/92) in view of Schinnick et al (US Patent No. 4,976,958), Dunn et al (WO 95/12676, May 11, 1995) and Flavell et al (WO 95/04145, Feb. 9, 1995).

Weigel et al teach that the 47 kDa surface antigen is useful in a serological test for syphilis (see page 1575) and teaches that the antigen is highly immunogenic or pathogenic (page 1568).

Schinnick et al teaches using a polymer of repeating *Mycobacterium tuberculosis* peptide units for use in an immune assay (see column 5).

Dunn et al teach chimeric *Borrelia* proteins (i.e. the instant fused antigen) consisting of at least two antigenic polypeptides form corresponding and/or non-corresponding proteins from the same and/or different species. Dunn et al teach that these chimeric proteins are useful as immunodiagnostic reagents.

Flavell et al teach that the antigenic polypeptides maybe expressed as fusion proteins and multimeric proteins from *Borrelia* (page 23, lines 5-11) for the objective of increasing stability or rendering the molecules more amenable to purification and preparation.

As to claims 26, 27 and 32-34, it would have therefore been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, to make repeating homopolymers of the known *T. pallidum* 47 kDa surface antigen of Weigel et al because each of Schinnick et al, Dunn et al and Flavell et al teach that homomeric/multimeric proteins are useful as assay reagents, increase the stability of the molecules and may render the molecules more amenable to purification and preparation and Weigel et al teach that the 47 kDa surface antigen is useful in serological assays syphilis. While none of the references teaches fusing specifically two, three or four of the same antigen together as recited, one of ordinary skill in the art would have been expected to optimize the number of linked units in the homopolymer to provide for a highly sensitive assay for the detection of antibodies or *T. pallidum per se*.

Status of the Claims

All claims stand rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 703-305-7555.

After January 27, 2004 the examiner can be reached at telephone number 571-272-0855 The examiner can normally be reached on M-F 9:30pm-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Smith Lynette can be reached on before January 27, 2004 at 703-308-3909, after January 27, 2004 at 571-272-0864. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patricia A. Duffy, Ph.D.
Primary Examiner
Art Unit 1645